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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,720	07/20/2006	Claude V. Maina	NEB-238-PUS	4742

28986 7590 10/29/2009  
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EXAMINER
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GIBBS, TERRA C

ART UNIT	PAPER NUMBER
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1635

NOTIFICATION DATE	DELIVERY MODE
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10/29/2009

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

STRIMPEL@NEB.COM  
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<p align="center"><b>Advisory Action</b> <b>Before the Filing of an Appeal Brief</b></p>	<b>Application No.</b> 10/586,720	<b>Applicant(s)</b> MAINA ET AL.	
	<b>Examiner</b> TERRA C. GIBBS	<b>Art Unit</b> 1635	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 13 October 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.  
 b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

#### AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
 (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
 (b) ☐ They raise the issue of new matter (see NOTE below);  
 (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
 (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
 5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.  
 6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
 7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
 The status of the claim(s) is (or will be) as follows:  
 Claim(s) allowed: \_\_\_\_\_.  
 Claim(s) objected to: 1 and 5.  
 Claim(s) rejected: \_\_\_\_\_.  
 Claim(s) withdrawn from consideration: 12-30.

#### AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
 9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
 10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

#### REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.  
 12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_  
 13. ☐ Other: \_\_\_\_\_.

/Terra Cotta Gibbs/  
October 22, 2009

/Sean R McGarry/  
Primary Examiner, Art Unit 1635

Continuation of 5. Applicant's reply has overcome the following rejection(s): The 35 U.S.C. 112, second paragraph rejection against claims 1 and 5 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is hereby withdrawn. The 35 U.S.C. 103(a) rejection against claims 1 and 5 as being unpatentable over Blaszczyk et al. in view of Sun et al. is hereby withdrawn.

Continuation of 11. does NOT place the application in condition for allowance because: Claims 1 and 5 would be objected to as containing nonelected subject matter, but would be allowable if rewritten to exclude the nonelected subject matter. Furthermore, claim 5 would be objected to because the claim is grammatically incorrect as the phrase, "at least 90% of the large dsRNA" is incomplete.

Claim 1 is considered to be free of the prior art since the prior art does not teach or fairly suggest a method comprising reacting a preparation of large double-stranded RNA (dsRNA) with an effective amount of a mutant RNase III in a magnesium- or manganese-containing buffer to produce a heterogeneous mixture of fragments in which at least 15% of the fragments have a size of 18-25 nucleotides, wherein the at least 15% of the fragments are not substantially degraded in the presence of the effective amount of the mutant RNase III for at least 1 hour, the heterogeneous mixture comprising heterogeneous short interfering double-stranded RNA (hsiRNA) suitable for silencing gene expression, the mutant RNase III comprising E38A in E. coli RNase III.

Claim 5 is considered to be free of the prior art since the prior art does not teach or fairly suggest a method comprising forming a heterogeneous mixture of fragments by incubating a large double-stranded RNA (dsRNA) with a mutant RNase III for an effective time for cleaving, in the presence of magnesium ions or manganese ions, where cleavage can be detected by gel electrophoresis and ethidium bromide staining, wherein at least 30% of the cleaved dsRNA has a fragment size of 18-30nt, the mutation in the RNase III comprising E38A in E. coli RNase III.